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URETERO-VENOUS ANASTOMOSIS
WITH OBSERVATIONS ON EXPERIMENTAL HYDRONEPHROSIS AND THE BLOOD NITROGEN

By Monr R. Reid,

Instructor in Surgery

(From the Hunterian Laboratory of The Johns Hopkins University)

In the course of some experimental work on the blood-vessels of dogs in which arterio-venous fistulæ were made in various situations, it occurred to me to test the effect of anastomosing the ureters with the venous system. I had particularly in mind the possibility that the kidneys might increase or decrease the toxicity of substances which they eliminate from the blood. In addition to this point, these experiments have permitted me to make some interesting observations on the mechanism of the production of hydronephrosis.

In connection with various problems a great deal of contradictory experimental work has been done on the kidneys and ureters of animals. Brown Séquard [1] thought that the kidneys possessed an internal secretion of great importance and even regarded uræmia as due more to the absence of it than to the retention of toxic substances. To a certain extent his idea has been supported by the work of Bradford [2] and others, but by Pearce,[3] who has removed as much as three-quarters of the total kidney substance without evident impairment to the body function, the presence of an internal secretion has been doubted. By many investigators [4, 7] the most marked hydronephrosis has been produced by only partial obstruction of the ureter, whereas others [5] have noted that complete has been as effectual as partial obstruction. Some [8] have observed the dilation in hydronephrosis to begin near the pelvis of the kidney and proceed toward the point of obstruction in the ureter, others [6] that the reverse occurs. The cause of the ureteral pressure in obstruction in the ureter and the effect of the pressure on the kidney secretion have received different interpretations from the various investigators.[7] Similarly, in many other problems regarding the kidney and ureter, interesting differences of opinion exist. Most work has had to do with a disturbance of the kidney function or the natural outlet for its secretion. And these experiments have only slight bearing on the big problems of chemistry involved in the study of diseased kidneys and experimentally impaired renal function, or with the transplantation of the ureters elsewhere than into the blood-stream.

Practically all investigators [2, 4, 5] are agreed that dogs usually die in from three to five days after a double nephrectomy or the ligation of both ureters, and that the ligation of one ureter is compatible with life for an indefinite period. Various transplantations of the kidney and ureter have been made, but, so far as I know, in dogs the effect on life of single and double uretero-venous anastomosis has not hitherto been attempted.

The chemical studies in these experiments were made in the laboratory of the chemical division of the medical clinic. For these data and for valuable suggestions I am greatly indebted to Dr. H. O. Mosenthal.

Technique

The method of anastomosis is shown in the accompanying illustrations (Vide Figs. 1, 2). In all the experiments the right ureter was introduced into the vena cava; when a double

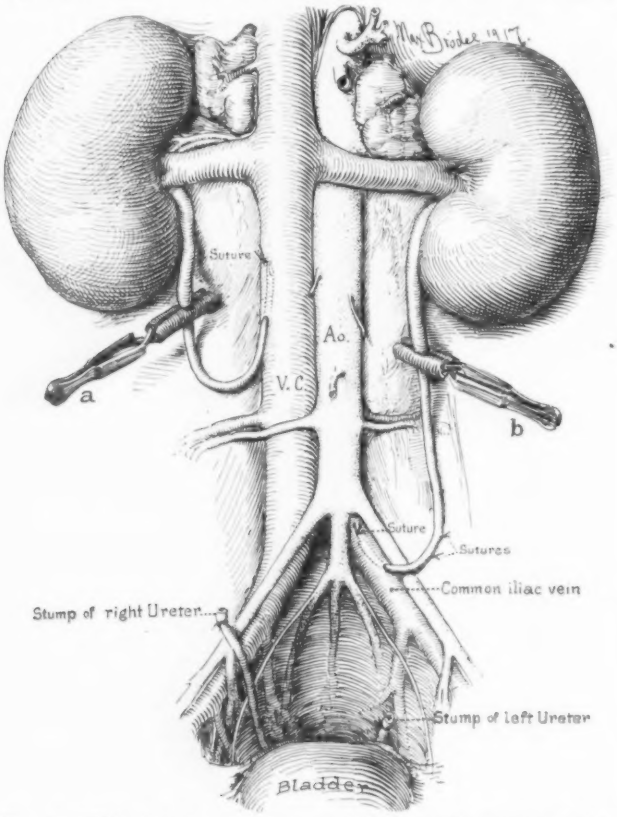

Fig. 1.—With clamps *a* and *b* removed, the uretero-venous anastomosis is complete. *V. C.* = vena cava. *Ao* = Aorta.

anastomosis was made, the left ureter, at a later period, was introduced into the left common iliac vein. The abdomen was entered either through the rectus muscle or through a transverse incision. The ureter was blocked at a point about 6 cm. from the pelvis of the kidney, by means of a Crile clamp, and considerable pressure was allowed to develop in the ureter by the time the anastomosis was completed. A segment of vein, 2.5 cm. long, was carefully freed and its blood-stream interrupted by temporary ligatures or clamps. Then an opening in the vein which the ureter would just fill was made, and through it the segment of the vein was washed free of blood with normal salt solution and albolene. The ureter was then divided obliquely, at such a distance from the bladder that it could be gently curved without kinking, and introduced into the vein in the direction of the blood-stream. Central to the opening for the ureter a half-curved needle, threaded with 00000 silk was introduced into the lumen of the vein and brought out through the opening. The pointed end of the ureter was then caught in the suture and the needle passed back through the foramen into the vein and brought through the vein wall close to where it was first introduced. After this mattress suture had been tied, the ureter was pulled into the vein lumen and sutured to its inner wall. The clamps were then removed and the blood allowed to resume its course. Rarely was it necessary to close the slit in the vein with a suture in order to prevent bleeding. Occasionally the adventitia of the ureter at the curve was sutured to the parietal peritoneum in order to prevent kinking of the ureter. All bleeding vessels were tied and all wounds closed with silk.

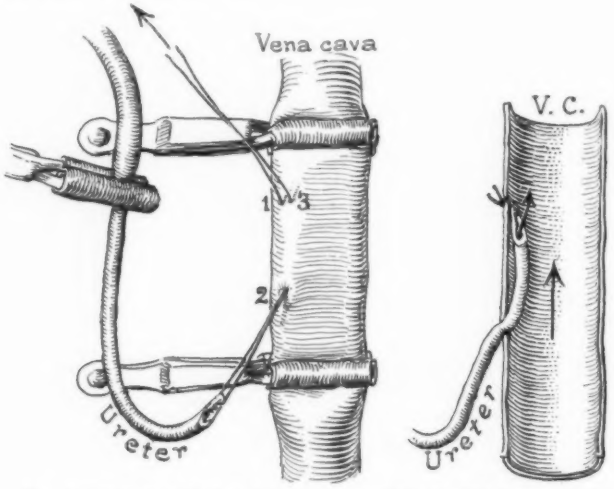

Fig. 2.—Numbers 1, 2 and 3 show the order in which the suture is made. To the right the ureter is shown sutured to the inner wall of the vein.

Experiments

The following are the complete protocols of the experiments with the exception of the chemical findings which are detailed further on:

Dog 1

May 1, 1917. Through a right rectus incision the right ureter is anastomosed into the vena cava. Before this anastomosis is made, blood is taken from the vena cava for chemical analysis.

May 2. The dog is in good condition; 10 c. c. of blood are taken from the jugular vein.

May 4. Except possibly for an increased thirst for water nothing abnormal is noted. The wound appears healthy and shows practically no reaction.

May 14. The wound has healed *per primam*. The general appearance is that of a normal animal. The appetite is good.

June 27. The condition of the animal seems to be perfect. There has been no apparent loss of weight. It has been nearly two months since the first uretero-venous anastomosis was made.

Second Operation.—Through a low left rectus incision the left ureter is anastomosed into the left common iliac vein. The right kidney on palpation seems a little large and somewhat cystic.

June 29. The dog is drowsy, but is apparently in fair condition. He is taking food and water very well.

June 30. The drowsiness is somewhat more marked. The animal still walks about and eats food.

July 4. For the past two days the dog has not eaten food and has been very drowsy. Death occurred this morning.

Autopsy.—There is a slight superficial infection of the wound but no peritonitis is present. The entire right ureter is markedly dilated and tortuous. The left ureter is dilated for a distance of about 2 cm. above the point of the anastomosis. The vein at both points of anastomosis is patent, and no clot formation is present. The intravenous part of the right ureter is dilated; the end of the ureter sticks close to the vein wall and is patent. Light pressure on the kidney or ureter forces urine into the vena cava. The end of the left ureter is open and fluid injected into the ureter flows readily into the vein.

The right kidney shows a very marked grade of hydronephrosis without any sign of infection. The pelvis of the kidney contains what is apparently clear, normal urine. The somewhat thinned cortex shows a normal gross picture. The left kidney is slightly swollen and injected, but there is no dilation of the pelvis. A little urine, which appears to be normal, is present in the pelvis. The capsule of both kidneys strips readily. In neither ureters nor kidneys is there any blood.

Weights:

Dog	13.5 kilos
Heart	140 grams
Right kidney	85 "
Left kidney	75 "

Histology of Kidneys.—Right kidney: The glomeruli appear to be normal. The collecting tubules stand out prominiently and appear to be somewhat dilated. They contain no albuminous material nor red blood cells. The epithelium of the convoluted tubules is practically normal. The nuclei stain well. There is no fibrous tissue increase. There is no polymorphonuclear nor round-cell infiltration.

Left kidney: The only possible abnormality suggested in the sections is an occasional slight swelling of the tubular epithelium and the presence of a small amount of albuminous material in the tubules.

Dog 2

May 2, 1917. Through a transverse incision the right ureter is anastomosed into the vena cava.

May 7. The condition of the dog is excellent. She takes food well and shows no evidence of a toxic condition.

May 14. The wound has healed *per primam*. Condition is excellent. Animal takes food and water well.

June 27. The dog is in perfect health.

Second Operation.—Through a low left rectus incision the left uretero-venous anastomosis is made.

June 29. The dog is drowsy, but walks about and eats perfectly well. There is no unusual sweating. Œdema is not apparent.

June 30. The condition is about the same as yesterday.

July 5. For the past two days the dog has practically not eaten and has been very toxic. It died this afternoon.

Autopsy.—The animal is still warm. Both wounds are perfectly healed and there is no infection.

An organizing thrombus occludes the vena cava from the point of the first anastomosis down for a distance of 3 cm. Below this a fresh ante-mortem clot extends down to the bifurcation of the vein and into the left iliac to the point of the last anastomosis. This thrombus does not occlude the vessel.

The right ureteral orifice is pervious and empties into the vein just above the point of occlusion by the thrombus. The entire right ureter is dilated and tortuous. Pressure on this or on the pelvis of the kidney causes urine to pass into the vein.

The left ureteral orifice is open and water injected into the ureter passes readily into the vein. This ureter for 3 or 4 cm. above the anastomosis is dilated.

There is a marked hydronephrosis of the right kidney which contains apparently normal urine.

The left kidney, except for slight œdema and injection, appears to be normal.

Weights:

Dog	13.7 kilos
Heart	150 grams
Right kidney	75 "
Left kidney	80 "

Histological Examination.—Right kidney: Section shows a moderate dilation of the tubules, a moderate degree of swelling of the convoluted tubules and occasionally a somewhat atrophied glomerulus. No hemorrhage, no polymorphonuclear nor round-cell infiltration. The nuclei stain well. No thickening of the blood vessels is apparent.

Left kidney: The only deviation from the normal suggested in the section is a slight swelling of the tubular epithelium.

Dog 3

May 3, 1917. Through a transverse incision the right uretero-venous anastomosis is made.

May 7. The dog is bright, playful, and eats.

May 14. The wound has healed *per primam*. The animal seems to be in perfect health.

June 29. The single anastomosis has apparently not affected the health of the dog.

Second Operation.—Through a low left rectus incision the left uretero-venous anastomosis is made. To palpation the right kidney is large and soft.

June 30. The dog takes food and water. Seems to be a little drowsy.

July 6. The drowsiness increased; the appetite for food and water disappeared, and the dog died this morning.

Autopsy.—The wounds are clean. There is a marked hydronephrosis of the right kidney. The pelvis is distended with a cloudy urine. It is injected and fibrin is deposited in the calices of the kidney. The capsule of the kidney strips readily. The cortical striations are not very regular. The right ureter is markedly dilated and tortuous. The end of the implanted ureter is not pervious, but is grown over by a smooth intima. The intravenous portion of the ureter forms a little pouch projecting into the lumen. Pressure on the pelvis of the kidney or the ureter does not force fluid into the vein.

The left ureter is patent and water injected into it passes readily into the vein. The ureter is dilated near the point of the anastomosis. The left kidney seems to be practically normal except for a possible slight dilation of the pelvis.

Weights:

Dog	12 kilos
Heart	150 grams
Right kidney	80 "
Left kidney	75 "

Histological Examination.—Right kidney. The section shows an extreme grade of chronic diffuse nephritis characterized by an extensive proliferation of connective tissue with corresponding compression atrophy, and obliteration of the tubular elements. The glomeruli show thickened capsules but no adhesions between the capsules and tufts, and obliterative changes in the vessels. Isolated areas of mononuclear and polymorphonuclear infiltrations are found, especially in the region of the pelvis, but these are not a prominent feature.

Left kidney: The tubular epithelium is swollen and in some areas there is a suggestion of early degenerative changes. No infection. No fibrosis.

Dog 4

May 3, 1917. Through a transverse incision the right ureter is anastomosed into the vena cava.

May 7. The dog does not appear to be drowsy. He takes food and water well.

May 14. The wound has healed *per primam*. The condition of animal is excellent.

June 29. The animal seems to be in as good condition as before the anastomosis was made.

Second Operation.—The left uretero-venous anastomosis is made.

June 30. The dog seems to be a little toxic but is otherwise in fair condition.

July 3. Death rather unexpectedly about noon to-day. The dog ate his breakfast and drank some water.

Autopsy.—The vein is normal in appearance. The mouth of the right ureter is easily seen. Pressure on the ureter or hydronephrotic kidney causes urine to empty into the vein. The pelvis of the right kidney contains urine which appears to be normal.

The left ureter is slightly dilated just above the point of the anastomosis. The anastomosis is also patent. The left kidney appears to be practically normal.

Weights:

Dog	9.9 kilos
Heart	140 grams
Right kidney	50 "
Left kidney	70 "

Histological Examination.—Right kidney: The epithelium is low. The ducts are somewhat dilated. No evidence of infection.

Left kidney: There is some swelling of the tubular epithelium and at the pelvis a small area of leucocytic infiltration.

Dog 5

Nov. 7, 1916. Through a right rectus incision the right ureter is anastomosed into the vena cava.

Nov. 15. The wound healed *per primam* and the dog seemed to be in excellent condition yesterday. Death occurred during the night.

Autopsy.—The wound and peritoneal cavity are free of infection. Death was due to intestinal intussusception at the ileo-cecal valve.

The right kidney is markedly increased in size, weighing 122 grams. It has a reddish black appearance. The capsule is œdematous and has a fibrous exudate over it. The right renal vessels are patent and normal. The capsule is stripped with difficulty, a rough red and white mottled surface being left. The pelvis is slightly dilated and contains a yellowish gelatinous material which extends in finger-like processes up into the calices. The pyramids are of a dark red color. The cortex is swollen and filled with hemorrhages. The striations are distinct. The glomeruli are easily seen.

The ureter is dilated and filled with a milky fluid. This passes readily into the vein through the pervious ureteral anastomosis.

The left kidney and ureter appear to be normal.

Histological Examination.—The right kidney shows an extreme grade of acute nephritis; many clumps of bacteria are present.

The left kidney shows no infection and a normal structure.

Cat 1

October 30, 1916. The right ureter is anastomosed into the vena cava.

Nov. 15. The cat seems to be perfectly normal.

Nov. 27. Death this morning.

Autopsy.—The body is well nourished. There is no œdema and no ascites. The ureter is slightly dilated and the lymphatics along it are distended. The kidney except for a little dilation of its pelvis appears to be normal. The ureteral opening is patent and fluid passes readily into the vein. No thrombus is present in the vein.

The left kidney is normal.

The right kidney weighs 13.5 grams, the left 15 grams. No cause for the death of the cat is found.

The hydronephrosis in these cases certainly resulted from a partial obstruction to the ureters. On the right side where the uretero-venous anastomosis had existed for two months the kidney in every animal showed a marked grade of hydronephrosis which involved the entire ureter and the pelvis of the kidney. On the left side, where the duration of the anastomosis was from four to six days, the ureter for a short distance above the anastomosis was dilated, whereas the pelvis of the kidney was only slightly, if at all, dilated. (Vide Figs. 3, 4 and 5).

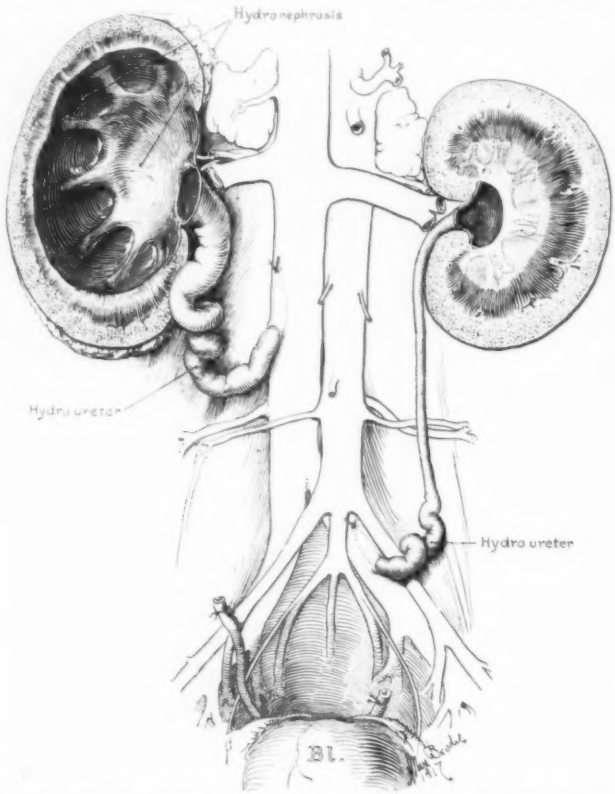

FIG. 3.—Hydroureter and hydronephrosis after uretero-venous anastomosis. The right dilation has developed in about two months, the left hydroureter in six or seven days. Note the ascending dilation on the left.

It is impossible to say whether the dilation resulted from a partial narrowing of the ureteral orifice, which was not very evident, or to the resistance of the venous blood stream. It has been shown by Keith and Snowden[5] that hydronephrosis will develop when a ureteral pressure of from 10 to 30 c. c. of water is established by partial obstruction in the ureter. When the ureteral pressure does not exceed 50 c. c. of water, a polyuria with definite modification in the character of the urine excreted develops. The kidney secretion is not totally sup-

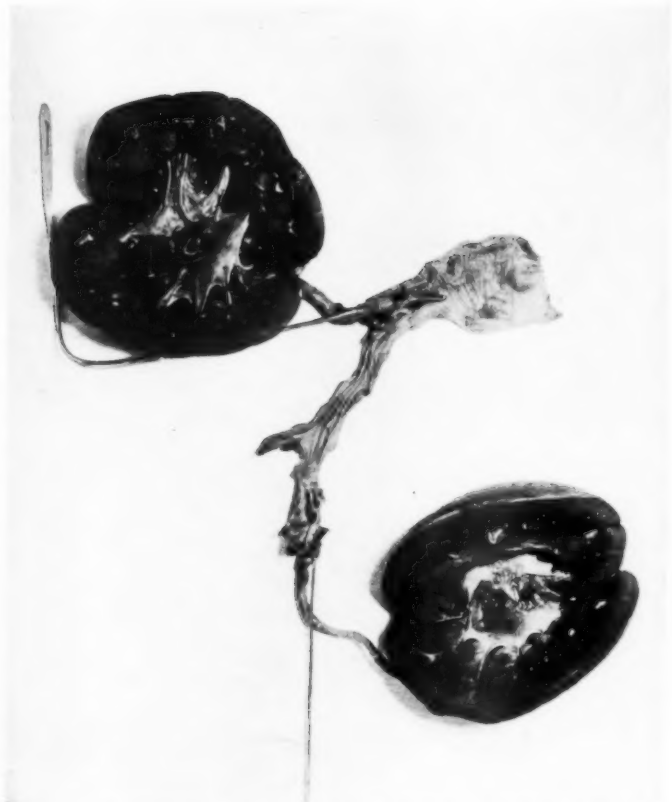

FIG. 4.—Photograph of the kidneys of dog 1. Specimens fixed in formalin. Duration of the right anastomosis two months and three days, of the left seven days. Both anastomoses are patent.

FIG. 5.—Photograph of the formalin-fixed specimen of dog 4. Duration of the right anastomosis two months, of the left five days. Both ureters are patent. There is no thrombosis. Note the hydroureter and hydronephrosis.

pressed until the enormous ureteral pressure of above 50 mm. of mercury is present. Bayliss and Starling[9] have found the normal vena cava pressure to vary between 2.5 and 7 mm. Hg. In the left femoral vein Burton-Opitz[10] found the pressure to be 5.39 mm. Hg. It has been shown[11] that the inferior vena cava pressure varies with the abdominal pressure so that both remain the same. The opening of the abdominal cavity certainly alters the venous pressure. It may be that the constant low pressure in the vena cava is sufficient to produce the hydronephrosis.

In Dog 3, who had a complete obstruction to the ureter, there was a high grade of hydronephrosis, associated with a marked fibrosis of the kidney substance. The belief, based erroneously on the work of Cohnheim[12] and other experimenters,[13] is that atrophy of the kidneys follows complete ligation of the ureter. More recent investigators,[14] however, have obtained opposite results and report hydronephrosis following complete ligation of the ureter. The dilation in Dog 3 may have resulted before the ureter became totally occluded. Yet the extreme fibrosis here, as compared with the other hydronephrotic kidneys, may indicate that in complete ureteral ligation hydronephrosis does result, but that the kidney tissue rapidly becomes functionless and following the absorption of the urine in the pelvis, ultimately becomes contracted.

The results of our experiments are not confirmatory of the observations of those who believe that hydronephrosis begins near the pelvis of the kidney and descends toward the point of obstruction. In every instance the left ureter, which had been transplanted for only four to eight days, showed a dilation for a short distance above the anastomosis, but not in the renal end of the ureter and probably not in the pelvis.

Chemical Studies.—At frequent intervals, specimens of the blood were analyzed for their non-protein nitrogen and urea content. At autopsy the muscle was similarly studied, and a specimen of urine from the pelvis of each kidney was examined.

The total non-protein nitrogen was determined in the filtrate after precipitation with trichloracetic acid, the method advocated by Greenwald[15] being used, except for the omission of the second precipitation with kaolin which was not found to be necessary. This procedure yields higher results than the use of alcohol as advocated by Folin and Denis[16] and in our experience has yielded data which are more nearly correct. The urea nitrogen was estimated according to Marshall.[17] The salt in the urine was estimated by the Volhardt method, and the nitrogen by the Kjeldahl process.

TABLE I

	Duration of Anastomosis	Fistula	Infection	Hydronephrosis	Weight of Kidney	Histology
Dog 1						
Rt. Kidney.....	63 days	Patent.	None.	Marked, involving pelvis and entire ureter.	85	Practically normal
Lt. Kidney.....	7 days	Patent.	None.	Present only in distal end of ureter.	75	Normal.
Dog 2						
Rt. Kidney.....	63 days	Patent.	None.	Involves pelvis and entire ureter.	75	Almost normal.
Lt. Kidney.....	9 days	Patent.	None.	Only the ureter and near anastomosis.	80	Normal.
Dog 3						
Rt. Kidney.....	63 days	Not Patent	Present.	Marked in pelvis and ureter. Pus present in urine.	80	Chronic diffuse nephritis, extensive. Moderate infection.
Lt. Kidney.....	7 days	Patent.	None.	Only in distal end of ureter.	75	Normal.
Dog 4						
Rt. Kidney.....	60 days	Patent.	None.	Marked in pelvis and ureter.	50	Epithelium low. Some dilation of ducts. Very little change from normal.
Lt. Kidney.....	4 days	Patent.	None.	Slightly dilated just above point of anastomosis.	70	Some swelling of tubular epithelium.
Dog 5						
Rt. Kidney.....	8 days	Patent	Present.	Ureter œdematous and dilated; pelvis only slightly.	122	Extreme grade of acute nephritis.
Lt. Kidney.....	Not done	.....	.....	None.	.....	Normal.

The upper limit of normal for the non-protein nitrogen of the blood under usual conditions of diet is about 40 mgm. per 100 c. c. and 15 mgm. for the urea nitrogen. This is true for human beings[18] and in our hands these figures have been equally applicable to dogs. After the first uretero-venous anastomosis the non-protein nitrogen of the blood is at the upper normal limit, exceeding it by a slight margin at times. It varied between 32 and 53 mgm. per 100 c. c. of blood for the first two weeks after operation. The blood urea nitrogen was also slightly increased during this period, varying between 13 and 26 mgm. At the end of two months the urea nitrogen varied between 11 and 18 mgm. Such a minimal increase may be regarded as due to the passage of the urine from the right

kidney into the veins and the inability of the left kidney alone to maintain an absolutely normal level of waste products in the blood during the first two weeks, and to the fact that subsequently it functionated more efficiently.

When the second uretero-venous fistula was complete, both the total non-protein nitrogen and the urea nitrogen of the blood rose at a very rapid rate, much as they do in dogs in which bilateral nephrectomy has been performed. Under the latter condition, in three experiments, the urea nitrogen in the blood at autopsy was found to vary between 232 and 321 mgm. These figures are comparable to those of 349 to 523 mgm. for the total non-protein nitrogen and 222 to 376 mgm. of urea nitrogen found in the present series. The duration of life in these three nephrectomized animals was from four to six days, a period of approximately the same length as after double uretero-venous anastomosis. It would appear therefore that the results obtained in both, in regard to the rate of urea accumulation in the blood and the length of life of the animal, are the same whether a complete nephrectomy is done or the kidneys remain intact and excrete urine into the blood stream. These experiments indicate that the waste products of the blood in their passage through the kidneys are not rendered less toxic, nor is the urea changed chemically. It may be that some of the other waste products of the blood, such as the creatin, amino-acids, etc., may be modified in passing through the kidneys; however, the data thus far obtained are not conclusive on this point and must be verified before any definite statement can be made regarding them.

The urine analyses as shown in Table II present some interesting features. Dogs 1 and 2, in which there was no infection of the pelves of the kidney or the ureter, showed a very low concentration of salt and a comparatively high nitrogen content. This was true for both kidneys, for the side on which

TABLE II.—ANALYSES OF THE BLOOD AND MUSCLE SHOWING THE EFFECT OF URETERO-VENOUS ANASTOMOSES

(Values are given in milligrams per 100 c. c. of blood or 100 grams of muscle.]

Dog 1

	Blood												Muscle
	5/1	5/1	5/2	5/7	5/10	5/15	6/27	6/27	6/30	7/2	7/4	7/4	7/4
Non-Protein Nitrogen	30	Anastomosis, right	42	39	36	46		Anastomosis, left			Autopsy	446	585
Urea Nitrogen	8		24	23	18	22	13		138	238		305	255

Dog 2

	Blood											Muscle
	5/2	5/3	5/7	5/10	5/15	6/27	6/27	6/29	7/2	7/5	7/5	7/5
Non-Protein Nitrogen	Anastomosis, right	35	36	32	40		Anastomosis, left			Autopsy	523	460
Urea Nitrogen		19	16	13	22	18		88	219		376	225

Dog 3

	Blood										Muscle
	5/3	5/4	5/7	5/10	5/15	6/29	6/29	7/2	7/6	7/6	7/6
Non-Protein Nitrogen	Anastomosis, right	42	33	36	39		Anastomosis, left		Autopsy	400	505
Urea Nitrogen		24	15	15	23	11		167		308	218

Dog 4

	Blood										Muscle
	5/3	5/4	5/7	5/10	5/15	6/29	6/29	7/2	7/4	7/4	7/4
Non-Protein Nitrogen	Anastomosis, right	53	40	40	41		Anastomosis, left		Autopsy	349	468
Urea Nitrogen		26	19	17	19	12		196		222	170

there was a distinct hydronephrosis as the result of a ureterovenous anastomosis of two months' duration as well as for the kidney in which these conditions had only obtained for a few days. This would indicate that the urine secreted against pressure was not normal, but resembled that found in passive congestion of the kidneys.[19] A study of the urine in dogs when the hydronephrosis is produced by a ureteral pressure of 12 to 30 cm. of water shows a "polyuria, trace of albumin, diminished output of phenolsulphothalein and delayed excretion of lactose."[8] Under almost similar conditions Lépine and Porteret[2] and Schwartz[21] found that the concentration of urea nitrogen and sodium chloride was less than in normal urine,

TABLE III

Analyses of urine collected from the pelves of the kidneys at autopsy

	Amount of urine		Right		Left		Remarks
	Right	Left	NaCl %	N %	NaCl %	N %	
Dog 1	75 c.c.	About 5 c.c.	.06	1.09	.02	.97	Pus in pelvis of right kidney (Dog 3). Ureter not patent. Albumin, 6 grams per liter.
Dog 2	119 c.c.	About 5 c.c.	.04	1.20	.05	1.20	
Dog 3	33 c.c.	Small amount	.51	.48	....	....	

whereas Lindemann[22] observed that the sodium chloride remained unchanged. In human beings the character of the urine varies markedly with the degree of hydronephrosis and its cause. It may be normal;[23] the urea and sodium chloride content may be greatly reduced. It is not possible that there was an exchange of substances by diffusion between the urine in the pelves of these kidneys and the blood, as the concentration of both salt and nitrogen in the two fluids is vastly different.

Furthermore, it would appear that Dogs 1 and 2, in which the ureter was patent, had a urine of entirely different composition from that of Dog 3, in which the ureteral opening was closed. The considerable amount of pus, mucus and albumin (6 grams per liter) distinguished this last urine from the former ones; the concentration of salt was much higher and that of nitrogen much lower, indicating that the urine was excreted under entirely different conditions when the ureterovenous anastomosis was patent than when it was closed, and that in all probability some urine was passing into the blood stream while the ureter was open.

The average duration of life for dogs after a double nephrectomy or a double ureteral ligation is from four to five days. In this series it was 6¾ days after the second ureter was anastomosed into the venous system. The dogs became drowsy and toxic, and for a short time before death refused to eat or drink. Marked œdema before death was not noticed in any case. At autopsy one dog presented moderate œdema of both legs and body.

CONCLUSIONS

1. The technique by which uretero-venous anastomosis may be successfully accomplished, allowing of a ureter which remains patent, is described.

2. After anastomosis of the ureter into the vena cava the blood does not flow back into the pelvis of the kidney.

3. By anastomosing a ureter into the portal or splenic vein the effect of the urine on these organs could be studied.

4. Uretero-venous anastomosis leads to hydronephrosis unaccompanied by marked histological changes in the kidney the effect of the urine on these organs could be studied.

5. The dilation of the ureter in these cases begins at the point of anastomosis and ascends to the pelvis of the kidney.

6. After a single anastomosis, the life of the dog, at the end of two months, remains unaffected. The urea and non-protein nitrogen of the blood rises slightly at first but show no tendency to increase subsequently. When both ureters have been anastomosed into the systemic venous current, the blood urea and non-protein nitrogen continue to rise until death, about as rapidly as they do in cases of double nephrectomy.

7. The hydronephrotic kidney secretes urine which is characterized by a low salt and a high nitrogen concentration.

8. After double uretero-venous anastomosis the average life of the dogs in this series was 6¾ days. The kidneys apparently do not reduce materially the toxicity of the substances which they remove from the blood stream.

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OBSERVATIONS ON BIRD MALARIA AND THE PATHOGENESIS OF RELAPSE IN HUMAN MALARIA[1]

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The study of infectious diseases in certain of the lower animals has given us a large amount of information regarding infectious diseases in man; and this has been especially so in the case of infections with protozoa and worms. By taking advantage of the parallelism of such infections in man and the lower animals one has a constant supply of fresh material, and can carry out inoculation experiments which are important in study as well as in teaching.

In the study of human malaria, important information has been obtained from the study of bird malaria. Ross worked out the cycle of Proteosoma in mosquitoes when it was not convenient for him to work on human malaria. MacCallum first observed the fertilization of the macrogamete by the microgamete in Hæmoproteus. In both cases the work was later confirmed for the human malarial parasites.

My object in undertaking this study was to try to correlate the points we know in the life cycles of various parasites of the red blood cells; and to try, in that way, to get an explanation of relapse in human malaria. Proteosoma closely resembles the human malarial parasites, and it is convenient to work with; for these reasons I chose Proteosoma for my work.

Bird Malaria

From the work of Schaudinn, Novy and MacNeal, the Sergents, and Aragao, it appears that more than one type of life cycle may be included in the present genus Hæmoproteus. Aragao's work has given us an understanding of the cycle of Hæmoproteus columbæ in the vertebrate host.

In Hæmoproteus columbæ schizogony takes place in the leucocytes (or endothelial cells) in the internal organs, especially in the lungs. Only gametocytes are found in the red blood cells; a bird once infected is proof against further infection; and the infection is not transmissible by injection of blood. The infection is transmitted by a hippoboscid fly.

Thus we see that while Hæmoproteus is well suited for studying the behavior of the gametocytes, it differs from human malaria where both the schizonts and gametocytes are in the red blood cells, and the disease is transmissible by injection of blood.

On the other hand, Proteosoma is like the human malarial organism, in that the schizonts and gametocytes are in the red blood cells, the infection is transmissible by injection of blood, and the intermediate host is a mosquito.

In the earlier study of Proteosoma it was considered that the schizonts persisted for a considerable time, but that they finally disappeared and the bird was immune.

Wasielewski showed that the schizonts persisted in the blood for from 3 to 5 or even from 9 to 11 months, because it was found possible to transmit the infection by injections of blood up to that time. From a bird in which parasites could not be found in the peripheral blood, 0.15 c. c. of blood divided among three birds infected only one. Wasielewski also found that the parasites were more numerous in the heart's blood than in the peripheral circulation.

Moldovan showed that occasionally birds recovered as early as one month after injection, but that usually there was a chronic infection up to six months with all stages of the parasite in the peripheral blood.

One of my problems was to determine whether the parasites were constantly in the peripheral blood in a form in which the infection could be transmitted by injections of blood; and, if so, how long they remained there.

The work was done with a strain of Proteosoma that was obtained from sparrows in New York in August, 1913, and has been carried in canaries up to the present time. This strain was obtained and used primarily for teaching purposes.

The method of procedure was to take blood from a wing vein of the infected bird, dilute it with physiological salt solution and inject it into the thoracic cavity and into the breast muscles of a clean bird. Parasites can be found in the peripheral blood up to four or five months after infection:

[1] Read at the meeting of The Johns Hopkins Medical Society, December 3, 1917.

after that I have rarely succeeded in finding them. But peripheral blood from an infected bird, when injected into a clean bird, has always transmitted the infection. Peripheral blood taken from a number of infected birds from month to month and injected into clean birds has not once failed to infect. The longest I have been able to follow the infection in any birds was in three birds for 29 months from the time of their infection. These birds were injected on May 14, 1914, and the last transference of blood from them was on October 12, 1916. During this time, many birds were injected with blood from the wing vein of these birds, and in every case the injected bird became infected. All birds injected with blood from these birds on the latter date became infected. All three of the old birds died before the time for another blood transference.

From this work it appears that the parasite of bird malaria is constantly in the peripheral circulation in a form which will transmit the infection on direct injection into clean birds; and that this form of the parasite is present for at least 29 months after infection.

IMMUNITY

Bound up with this is the question of immunity. Koch, Ruge and others were of the opinion that one attack of Proteosoma infection conferred immunity, and that the increase in number of cases of the disease in the spring could not be accounted for by relapses.

Wasielewski did not agree that there was immunity. After the injection of blood from infected birds into birds whose peripheral blood had been free from parasites for 4 days, 14 days, 3 months and 9 months, he was able to find on the fifth day a few parasites in the peripheral blood of the supposedly recovered birds. In three birds the number of parasites was so small that it was even possible they were only the injected parasites: the fourth bird showed from 20 to 30 parasites in specimens taken from the eleventh to the fourteenth day. Wasielewski was not sure whether the case was one of a mild relapse or of a mild new infection; but he did consider that it showed the bird was not immune.

Moldovan showed that recovered birds were susceptible to infection just as much as birds that had never been infected, but chronically infected birds were resistant against superinfection.

RELAPSE

In chronically infected birds there is not much change in the number of parasites in the peripheral blood, and spontaneous increase of the number of parasites has not been observed. Wasielewski often noted an increase in the number of parasites in the blood of his birds during intercurrent infections of some other sort.

Moldovan was able to produce relapses by the injection of blood of rice-birds; it made no difference whether or not there were parasites in the blood of the rice-birds.

In Wasielewski's experiments which he considered as showing that there was no immunity in recovered birds, he got only a few parasites in the peripheral blood of the supposedly recovered bird after an injection of Proteosoma material. But Moldovan showed that recovered birds developed a rich infection and in the usual time, just as did fresh birds, after an injection of Proteosoma material.

I injected blood from one 29-month infected bird into another 20-month infected bird. On the twentieth day one parasite was found in the peripheral blood of the injected bird. A previous injection of blood from each bird into a clean bird showed that the peripheral blood of both birds contained Proteosoma in a form that would transmit the infection to clean birds in the usual way.

One bird, which had been injected with Proteosoma four months previously, showed one partly grown parasite in the peripheral blood in a 10-minute search with a 1/12″ objective. This bird was given an injection of blood from a clean bird. On the fifth day this bird showed no parasites in the peripheral blood on a similar search; on the twelfth day it showed one parasite in the peripheral blood on a similar search: this bird died on the seventeenth day, before another examination was made.

At the same time, the clean bird used in this experiment was given an injection of blood from the infected bird used in this experiment. On the fifth day this bird showed no parasites in the peripheral blood in a 10-minute search with a 1/12″ objective; on the twelfth day it showed a few parasites in the peripheral blood; and on the seventeenth day there was a rich infection.

One bird that had been injected with Proteosoma four months previously showed no parasites in the peripheral blood in a 10-minute search with a 1/12″ objective. This bird was given an injection of human blood. On the fifth and twelfth days it showed no parasites in the peripheral blood on a similar search: on the seventeenth day there was a fair number of parasites in all stages of development in the peripheral blood.

One bird that had been injected with Proteosoma 21½ months previously showed no parasites in the peripheral blood in a 10-minute search with a 1/12″ objective. This bird was given an injection of human blood. On the fifth, twelfth and seventeenth days, this bird showed no parasites in the peripheral blood in a 10-minute search with a 1/12″ objective.

SUMMARY

Thus it appears: (1) that in Proteosoma the usual thing is for the bird to develop a chronic infection which may last at least 29 months; (2) that all stages of the asexual cycle are found in the peripheral blood as long as any parasites are found there; (3) that the parasites are constantly present in the peripheral blood for at least 29 months in a form that will transmit the infection by the injection of blood; (4) that relapse occurs as a result of lowered resistance from intercurrent infections, or of the injection of foreign blood; and (5) that immunity lasts only as long as the bird remains infected.

Discussion

Is the asexual cycle present in the peripheral blood throughout the infection? Since the asexual cycle is present as long as we are able to find any parasites, it is very probable that it is there throughout, but is not found on account of the shortcomings of our methods of direct examination.

Then, the fact that the infection is transmissible throughout the course by the injection of peripheral blood makes it probable that the asexual cycle is present in the peripheral blood throughout the infection. In a Hæmoproteus infection, in which schizogony takes place in the internal organs and only the gametocytes are present in the peripheral blood, the infection is not transmissible by the injection of blood. The same difference holds for Babesia and Theileria: in Babesia the schizogony takes place in the red blood cells, and the infection is transmissible by the injection of peripheral blood; while in Theileria the schizogony takes place in the internal organs, only the gametocytes are present in the peripheral blood, and the infection is not transmissible by the injection of blood. We shall get some further help on the question from a study of human malaria; and the question of some special or resistant form of the parasite can be taken up then.

Human Malaria

When we come to study human malaria, we do not have the assistance of animal inoculations. But we are able to study the peripheral blood some months after the last attack of malarial fever; and in this way we may get at the question of whether the asexual cycle continues during the period between relapses.

It is not unusual to find gametocytes in the blood of man several months after the last attack of malarial fever; and as a result of finding parasites in the blood of men in the spring, before mosquitoes are able to transmit them, we have come to the belief that man and not the mosquito carries the malarial parasite through the winter. Gametocytes are commonly found in the blood of these "carriers" in the spring; and it is generally agreed that the gametocytes are intracorpuscular.

Rowley-Lawson holds that the human malarial parasites are extracorpuscular and that they migrate from one red cell to another. The sporozoa are intracellular parasites. Aside from the points in human blood that indicate the malarial parasites to be intracorpuscular, there are some points in other parasites of the red blood cell that would indicate that the malarial parasite is intracorpuscular. Proteosoma crowds the nucleus of the red blood cell to one side as it grows; Hæmoproteus curves around the ends of the nucleus of the red blood cell as it grows; the hæmogregarines curve around the ends of the nucleus of the red blood cell, coil up beside it, or crowd it to one side, as they grow.

The lowest estimate of the rate of death of the red blood cells would make the life of a red blood cell 55.5 days. Other estimates would make it as low as 23 days.

Since we do not believe that the gametocyte is able to travel from one red blood cell to another, we must conclude that any gametocyte found came from a schizont less than two months before. So, if gametocytes are found in the blood six or eight months after the last attack of fever we must conclude that the schizogony continued for at least four to six months after the last attack of fever.

Craig found malarial parasites in the spleen of patients who had died of some disease other than malaria, and in whom there were no symptoms of malaria. The parasites were undergoing normal schizogony in the spleen, but in numbers insufficient to produce clinical symptoms.

It appears, then, that in human malaria, just as in bird malaria, schizogony continues for a long time in the chronic infection. Whether the schizogony continues in the peripheral blood or in the blood in the internal organs makes no difference in the part it can play in relapse.

Theories of Relapse

There are several theories as to the pathogenesis of relapse in malaria.

(1) Schaudinn considered that relapse was due to parthenogenesis of the macrogametocytes which persisted in the blood and internal organs of the patient.

Moldovan says that he undertook his experiments in order to determine whether relapse was due to parthenogenesis of the macrogamete as claimed by Schaudinn. He says that the establishment of the continuation of the asexual cycle of Proteosoma in the chronically infected birds made it unnecessary for him to study the question further along that line.

In Proteosoma, the asexual cycle takes place in the peripheral blood, the infection is transmitted by injection of peripheral blood, relapse occurs, and there is no immunity.[2] In

[2] Since writing this I have read Sergent and Hempl's article in Bull. Soc. path. exot., 1917, X, 550, Sur l'immunité dans le paludisme des oiseux.

Proteosoma-containing material was injected intraperitoneally into five canaries, at least two and one-half years after their original infection. One of the birds developed a severe infection, as did two controls. In one of the injected birds, no parasites were found after the injection, in three of them an occasional parasite was found. Sergent and Hempl conclude that, in four of the birds, a relative immunity had persisted for at least two and one-half years.

It is my opinion that had they injected blood from the five canaries into other canaries, they would have found that the four resistant birds were still infected, *labile infection*, and the bird which developed a rich infection was the only one that had recovered from the infection of over two and one-half years before. The occasional parasites found in the blood of three of the resistant birds were the ones that regularly circulate in the peripheral blood of birds that have a labile infection, and the parasites were found as a result of the prolonged search made at this time; or there may have been a mild relapse as a result of the injury on making the injection.

Since superinfection is not possible in labile infection, which is so common in protozoan infections, failure to infect by injection of infectious material cannot be interpreted as meaning immunity in these infections. Recovery must be determined by injection of blood from the supposedly recovered bird into a susceptible bird.

The conditions as to immunity and reinfection in syphilis are parallel with the conditions here.

Haemoproteus columbæ, the asexual cycle takes place in the internal organs, only gametocytes appear in the peripheral blood, and the infection is not transmitted by injection of peripheral blood; the question of relapse or recovery with sterile immunity is not cleared up; but a bird once infected is proof against further infection.

In the family Babesiæ we have life cycles similar to those of Proteosoma and Haemoproteus columbæ, and here the question of relapse and immunity is worked out. In Babesia, the asexual cycle takes place in the peripheral blood, the infection is transmitted by injection of peripheral blood, relapse occurs, and there is no immunity; just as in Proteosoma. In Theileria, the asexual cycle takes place in the internal organs, only gametocytes appear in the peripheral blood, the infection is not transmitted by the injection of peripheral blood, relapse does not occur, and there is immunity.

Meyer, writing of African coast fever in cattle, says that it is impossible to infect a cow with blood containing gametocytes; that when an animal has had the disease, the gametocytes and developmental forms disappear from the blood and the organs; that such an animal is no longer a "carrier" of the parasites, and does not suffer relapse. These facts, he says, long known, are explained by Gonder's investigations, which show that parthenogenesis does not occur in Pirosoma parvum (Theileria parva). He says that, in this, Pirosoma parvum (Theileria parva) is an exception from all other known pirosomes.

Schaudinn's work has not been satisfactorily confirmed. And in Theileria, the only organism so far worked out in which it was possible to work with persisting gametocytes without confusion from a continuation of the asexual cycle, it has been necessary to note an exception to Schaudinn's theory.

(2) The theory of a resistant form of the parasite has been put forward by Celli, Craig, and recently by James. In none of its forms is this theory consistent with any idea that the resistant or resting organism is intracorpuscular, on account of the short life of the red blood cell. Again, since gametocytes appear in the blood for months after the last attack of malarial fever, we know that the asexual cycle is going on. If it is considered that the resistant form of the parasite is extracellular, or is in some cell other than the red blood cell, we can only answer that no evidence of such a form has been found in Theileria, the only organism so far worked out in which there is not confusion from a continuation of the asexual cycle.

James' statement of the theory of a resistant or resting stage is as follows:

1. In instances of true relapse, as distinguished from recrudescence, the first forms of the parasite present in the peripheral blood are large forms which, if seen during the course of an ordinary attack, would certainly be classed as gametocytes, though it might not be easy to say definitely to which sex they belong. These forms, and the pre-sporulating forms which follow them, are found before the patient has any symptoms, or is aware that an attack is impending.

2. In cases which relapse during, or very shortly after, vigorous quinine treatment by the mouth or intravenously, prolonged search of the peripheral blood may fail to show the presence of parasites, but examination of films of splenic blood may reveal, as if "encysted" in dehemoglobinized red blood corpuscles, (a) large forms resembling gametocytes with a voluminous nucleus; (b) similar forms with the nucleus divided into three or more separate blocks.

These are persistent forms upon which quinine given intravenously is inoperative, and, failing a better explanation, one assumes that they are the cause of the relapses, and that they are not gametocytes, but are asexual forms in which the parasite lays up during the intervals between true relapses.

If no parasite can stay in a red blood cell more than two months, it does not appear that we can accept James' suggestion that the parasite lays up in a red cell during the interval between relapse. He is probably right in saying that they are asexual organisms, but they must go through their cycle in less than two months or be lost.

James' description of these parasites sounds like Prowazek's statement regarding the parasites that are found in chronic bird malaria. Prowazek says that, while in chronic human malaria we find mainly gametes, in chronic bird malaria we also find young parasites of which one is not able to say whether they are young schizonts or gametes.

Moldovan's statement that if we can demonstrate the continuation of the asexual cycle we do not need to study the question of whether relapse is due to parthenogenesis of the macrogametocyte applies equally to the theory of a resistant or resting form of the parasite.

Intracorpuscular conjugation, as described by Craig, can be interpreted as a method of keeping the asexual cycle active as readily as a method of producing a resistant form of the organism. We know that asexual reproduction can go on for years in various protozoa, as shown especially for Paramœcium by Woodruff and Erdmann. The strain of Proteosoma with which I have worked has been carried for over four years without going through an arthropod host. That some nuclear rearrangement takes place seems to be very probable, and intracorpuscular conjugation of parasites may be of the same nature.

(3) Bignami states that—

in all probability relapses, whether at short or long intervals, or whether separated by lengthy periods of latency, should be considered from a single viewpoint: that is to say, as having the same genesis, depending on the persistence of the pyrogenous cycle. In one group of relapses the parasitic material that maintains the infection is represented by a minimum quantity of forms of the ordinary fever-producing cycle, often recognizable by an accurate microscopical examination, at least at some time in the course of the infection, which forms for a long time cannot attain the quantity or the virulence necessary to cause fever. Especially in those cases in which a series of relapses occur at longer or shorter intervals without quinine treatment, one should keep in mind the possibility that after a series of febrile attacks the organism acquires a certain immunity in respect to the pyrogenic action of the parasites; which immunity being transitory, as happens in other infections, it is attenuated or ceases after a certain period of apyrexia; whence the onset of relapse.

But there is also a group of relapses, in which the material, which maintains the infection during the period of latency, is represented by forms resistant to quinine, due to a process of selection under the action of the alkaloid, as occasion offers; it is not necessary to suppose that such forms differ morphologically from others as I, myself, more than once, have also thought.

In my opinion, all of the findings are in keeping with Bignami's view; that is, that the asexual cycle persists during the period between relapses; that during the period between relapses the organisms are present in too small number to produce symptoms or to be found in the peripheral blood; and that when something happens to reduce the resistance, this cycle becomes more active, and the organisms become numerous enough to produce symptoms and to be found in the peripheral blood.

The continuation of the asexual cycle over long periods in which there is no clinical malaria is undoubted. Relapse does not occur in infections with the only organism worked out under conditions where it is possible to observe persistence of gametocytes. No resistant or resting intracorpuscular form of the organism can exist for more than 50 to 60 days, on account of the short life of the red blood cell.

Bignami considers that there is some change in the biological properties of the organisms that carry on the low grade asexual cycle and are resistant to quinine. I believe that there is something more to the immunity of the host than "in respect to the pyrogenic action of the parasites." That is, I think there is more than immunity to the *paroxysmal toxin*. Schilling is of the opinion that the *paroxysmal toxins* do not have any appreciable antigenic action. In cases not treated, not only do the attacks of fever become milder and finally cease, but the parasites become fewer and fewer in the peripheral blood. This is readily followed in Proteosoma infection of birds, and is a common observation in human malaria. Then, in Proteosoma, the infected bird is resistant to superinfection, even though no parasites can be found in the peripheral blood. I believe that antibodies are produced which actually oppose the growth and multiplication of the parasites: that in some cases this opposition is strong enough to actually destroy the parasites and recovery results; that more commonly the opposition is not strong enough to destroy the parasites, but a few of them become resistant and keep up the cycle—what Schilling calls *labile infection* (Plehn's *tolerance*). Here the animal resists superinfection. When anything occurs to lower the resistance of the host, these parasites multiply rapidly and set up a relapse. Here, as in so many other protozoan infections, the antibody production continues only as long as the infection exists: as soon as the infection ceases, the stimulus to antibody production is withdrawn, and the animal is again susceptible to infection.

Conclusion

In malaria, the body produces antibodies which resist the multiplication of the parasites. But certain of the parasites become resistant to these antibodies (or to quinine) and continue the asexual cycle, the number of parasites, however, being too small to produce symptoms. When anything happens to lower the resistance of the body, these parasites are able to multiply rapidly and produce symptoms; that is, a relapse. The continuation of gametocytes is due to the continuation of the asexual cycle. As long as the infection continues, the body is stimulated to produce antibodies, and the infected person is resistant to superinfection; that is, there is a labile infection. There is no immunity after recovery: as soon as the infection is stopped by the antibody production, or by treatment, the stimulus to antibody production is withdrawn, and the person is susceptible to reinfection, just as though he had never been infected before.

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DISCUSSION

DR. MACCALLUM.—I want to congratulate Colonel Whitmore upon this splendid paper which puts the whole thing in a much clearer light than it was before. There were two or three points that struck me particularly. One was the reference to the question as to whether the parasites are intracellular or not. I am sure there is no possible doubt about that. You can see them inside the corpuscles, see them move inside the corpuscles, see them move the nucleus and see the corpuscle break and the parasite come out, sometimes dragging the nucleus out.

The question of relapse is a most important one. I gathered from Colonel Whitmore's paper that it is his opinion that the asexual cycle is the thing that is responsible for the relapse. Colonel Whitmore's statement about the inability of these organisms to superimpose themselves on an old infection is especially interesting. Does that mean that no amount of introduction of new parasites, even of the same character, in case resistance is lowered, will "take" in such a person? In that case it is interesting to consider what has happened in those persons who die of an acute attack of malaria. You almost invariably find there are signs of long continued infection. Are we to understand that in those cases there has been one infection from the very beginning, and that they died from an acute attack merely because through some indiscretion they have lowered their resistance and have become subject to an exacerbation of their original infection? If that is so, it would mean, I suppose, that a person can have only one infection, in fact is practically immune then except for his original malaria.

I might say a word about the existence of malaria in some of the countries I visited last year. It is *the* disease in those tropical countries, especially in the East Indies. I think that cholera, plague and leprosy sink into insignificance compared with malaria. In the Malay States, for example, I found that the coolie laborers died off at an astounding rate. The engineer of public works at Kuala Lumpur told me he was in the habit of hiring 100 coolies at a time, different kinds each time. For instance, he would start with 100 Chinese coolies; 85 per cent would died off in a few days' time and the rest would run away. He would then try Malays and so on, but 95 per cent was the average of deaths. I did autopsies in Singapore for about 17 days and in that time I had 11 cases of fatal malaria at autopsy. In all my previous life I had seen only four fatal cases. These 11 cases were chiefly of the æstivo-autumnal, or subtertian type, as the English call them. The material, microscopically, proved to be most interesting. They were apparently cases of massive infection. The intestinal mucosa showed the capillaries completely plugged with organisms. In the brain also the capillaries were found to be completely plugged with parasites. I suppose that was largely responsible for the coma in which these patients were plunged toward the end.

LIEUT.-COLONEL WHITMORE.—I was very glad to hear Dr. MacCallum express himself so definitely that the parasite is intracorpuscular. That is an important thing for our argument.

The question of superinfection seems to be rather a broad one. The idea seems to be that the body has developed antibodies, and only certain of the parasites have become resistant; and they are able to live and complete their cycle just balanced by the antibodies; that is, we have a labile infection. Wasielewski was not able to say definitely in three of his birds whether the parasites circulating in the blood might have been the ones he injected. It is generally considered that in the protozoa, superinfection is not possible so long as infection lasts.

The question whether a man can have malaria more than once in his life is not so easy. Koch applied his immunity idea to human malaria and considered that in malarial districts the children who had the disease become immune, and for that reason we did not have malaria in adults. I think it is definitely agreed now that that is not the case; but that in those people who have had malaria as children, chronic malaria persists and that is why they do not have malaria as adults. They have a chronic (or labile) infection and are resistant to superinfection.

I would hate to feel, however, that with all of our treatment we do not cure any cases of malaria. Moldovan showed that occasionally birds recover. Of course, we have followed Proteosoma in birds for only 29 months, and that is not a very long time in the life of a man. Whether a man may be infected for a few years, and then recover, is pretty hard to say. In malarial districts, a great many people seem to recover, but apparently many of them remain infected. If they do recover, they get another infection right away, and always keep one going. In one place in Colombia, where we had occasion to go to look into some supposed yellow fever, it happened to be convenient to get blood from 10 persons—men who had not had malaria for months. In four of those 10 we were able to find malarial parasites in the peripheral blood without prolonged search; so I am inclined to think that those people have an infection almost constantly.

THE PHYSICIAN'S APHORISMS: A MEDIÆVAL HEBREW SATIRE

By HARRY FRIEDENWALD

Hippocrates was greatly revered during the middle ages by the Jews. He was called the "Chief of Physicians" by Maimonides and he was spoken of as "The Saint" (*He-Hasid*). His works were variously put into Hebrew from Arabic or from Latin translations and they were provided with Hebrew commentaries.[1] It is an indication of their popularity that a Hebrew satire was written in the form of the aphorisms under the title "The Physician's Aphorisms."

The author was En Maimon Galipapa,[2] a Provençal, of whom nothing is known but that he wrote satires (probably in the latter part of the 13th century), the one just mentioned and "A Widow's Vow," and "The Contentions of a Wife."

[1] See Steinschneider, Hebraeische Uebersetzungen, Berlin, 1893, p. 688.

[2] Concerning authorship, etc., see Davidson, Sefer Shaashuim, p. 119.

These works have been edited and published under the title "Three Satires" by Prof. Israel Davidson (New York, 1904), from "a unique copy in the Bodleian Library at Oxford."

Following the form of the Hebrew translation of Hippocrates, in which each chapter opens with the "Amar Abucrat" (*i. e.*, "Hippocrates says"), each paragraph of the satire begins with the words "Amar oyeb" (*i. e.*, the "Enemy says"). The Hebrew style is that much in favor at that period—the use of Biblical expressions and phrases woven together.

In the translation[2] which follows there is no attempt to indicate the Biblical references excepting in the first paragraph.

The Physician's Aphorisms

Oyeb (the enemy) said: "I will pursue and overtake [Ex. XV, 9] the worthless physicians [Zach. XI, 17 "worthless shepherds"]; they rejoice with the joy of harvest (Isaiah IX, 3) and as one gayly tripping to the music of the flute (Isaiah XXX, 29), when they slay a man before his time (Job XV, 32) and he is cut off from his people (Leviticus XVII, 4) and his place knows him no more (Psalm CIII, 16). I will tell of their wicked ways, their evil shall be disclosed, they who bring misfortune upon misfortune (Job XVI, 14), they who are corrupting the world (I Samuel VI, 5). I will conceal my name, lest they should curse me, lest in a short while they should stone me (Exod. XVII, 4).

"Whoever reads one chapter of this every day will abide in safety, and without fear; he will find repose for himself when his head aches; and if he knows it by heart, it will be a cure for all his flesh."

Chapter I. Gate of Vanity

1. Oyeb said: "Life is vanity; labor is regarded with disfavor; they who should work, shirk; and time presses.' Practice distresses; the sick are foolish and put their trust in a physician, a heretic or an atheist; those that aid him are stupid, leaning toward crooked ways. There is a time for life and for death, for cure or for the shadow of death. There is no controlling God's action! Who will be rejected? Who will be spared?"

2. Oyeb said: "When one is ill let him not seek the physician; whether he be strong or weak, do not desire his remedies. Avoid his paths, be careful lest he visit you, for one dare not expect a miracle. He comes with haughtiness and arrogance in order to increase the trouble. Woe unto the patient with whom the physician comes in contact, for seven abominations are in his heart. He winks, he gestures with his fingers; to increase his fee is his only thought."

3. Oyeb said: "The foundation of medicine was brilliant wisdom and its ways were upright. Recently, however, new people have come: the present doctors, who have learned little, boast: 'We are wise and know all the secrets of science,' but they are ignorant and empty-headed. They only take the gold the silver, the coin. They corrupt and do evil, but how to do good they know not."

4. Oyeb said: "At the first visit of the physician he says: 'Why are you lying down? Arise if you wish that your illness and your aching shall pass away; avoid wine and lust; likewise eat no meat, and subdue the desire of your stomach; eat nothing but barley food, which is healthy for asses, or a little bread with lentils and soup.' So spoke the physicians who were gathered in Bene Berak, that the fever might vanish. But the fever increases with pain, like a blossoming flower. The physician will promise to cure, but there is no assurance."

5. Oyeb said: "The doctor makes great pretense; he draws the patient's arms once to the left and then to the right: he says to the pulse, that it is good, but he is as a blind man who gropes about at midday. Once he will say that the patient is leaping over mountains, then that he is walking in the plains [*i. e.*, he is constantly contradicting himself]; there is no truth in his words; he is not able to distinguish his right hand from his left!"

6. Oyeb said: "Concerning the color of the patient's urine, the fool will speak deception and falsehood and will tell many lies. He will ask to look at the color, to determine whether the sickness is in the body or in the bones, for 'his waters deceive not' [Isaiah LVIII, 11]. He shakes the urinal; he sees whether the sediment is above or at the bottom, and whether it is red. When its appearance is red, he will sentence to death; he will look at it with sadness. But if it is white and cloudy, he will likewise say there is no hope. He sees but darkness and chaos."

Chapter II. A Gate of Ridicule

1. Oyeb said: "There are four kinds of humors[3] which are the foundation of the man's constitution, to enable him to walk abroad with his staff (Ex. XXI, 19). The temperaments produced by these humors are eight, good and bad. Each of these is opposed to the other. If there is peace among them, the body is healthy, there is no need for the doctor, for drugs nor for remedies. But when one property rises against the other, then the person takes to his bed and his visage is marred."

2. Oyeb said: "There are three kinds of fevers; in the humors, in the limbs, and in the spirits, and from these the fever spreads either for life or death; likewise all disease and pain, whether cold or hot, arise from these. But it is not worth while to call the doctor to aid, for he will say to himself:

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[2] I desire to express my gratitude to Professor Davidson for his advice and his revision of this translation, as also to Dr. E. N. Rabinowitz, Dr. L. M. Palitz, and Dr. David Blondheim for their help.

[1] Compare with the words of Hippocrates' Aphorisms: Life is short and art is long; the occasion fleeting, experience fallacious, and judgment difficult. Compare likewise with "Sayings of the Fathers" (II, 20) The day is short, the work is great, the laborers are sluggish, etc.

[3] The four elementary juices in Hippocrates' medicine were blood, phlegm, yellow bile and black bile.

'I shall become renowned if the patient's life is saved;' yet he is ignorant and willing to do a wrong."

3. Oyeb said: "In a continuous or daily fever, all that the physician does is falsehood and pretense and in tertian and quartan and complicated fevers [he is guilty of] thousands and myriads of errors. But what does it matter to the physician whether the patient dies or lives, so long as he gets his fee; and the result of his work, let it be what it may."

4. Oyeb said: When one is very constipated, the physician puts a syringe in the rectum, and gives an injection without rule or measure, in order to separate the 'bitter waters' and the faeces; while the syringe is still in place, the doctor thrusts it further in; the patient cries aloud and cannot endure it, but the doctor says: 'Keep quiet, until the mass is out. Why shall you remain constipated? Wherefore shall you die before your time? Now you will be clean of all impurity, and you will sit in cleanliness in your house. Wherefore shall you remember the day of your going out [*i. e.*, your movement].'"

5. Oyeb said: "When one has diarrhœa, is couching down . . . . cannot find rest for himself, and he needs to go abroad; when cramps, pain and suffering come on, and he is afflicted with his excrement and his intestines are boiling and he fills one vessel after another, until his abdomen and flanks cleave to one another; then the physician comes, haughty and working wonders, and he says: 'To death with the movements of the bowels, for I will give a remedy and this will stop; then will [you] again become firm and harder than a rock.' But to the patient this is of no avail, as the everlasting running still continues. Then will he cry: 'Why does this one [doctor] come to increase my troubles; for he has not closed the doors of my belly?'"

6. Oyeb said: "When the head aches, and the pain is severe and the only thing is to lie abed and the patient cries: 'My head, my head, call the doctor, tell him about me; because of the headache, I am not able to taste and touch anything; there is darkness [about me] and no light! Oh, that some one might cast me into a pit or into the river, for it were better for me to die than to live; there is no hope for my desires!' And behold, there come two asses, two physicians, ignorant of most things. One puts his hand on the patient's forehead, and the other on the back of his head, and they cause the patient to become more frightened. One says this, the other says that; and the patient continues his wailing. Then they will say: 'We need our books to find a remedy for you, that you shall again be able to raise your head!' One anoints him with the oil of falsehood, the other gives him 'bitter waters' to drink; they will not rest until they lower him into the pit of hell and uproot him completely."

7. Oyeb said: "When one has earache, the physician will examine; then he will say that this is the illness; why should he lie? He stretches forth his hand to take his fee and place it in his pocket or his purse. Then he prepares his remedies one by one, with his instruments, ointments, and wicks; in case these do no good [for they are useless], he complains that it is the patient's fault, 'who did not hearken to my voice and did not incline his ear to me.' Then the patient will reply: 'Behold, I remembered you when I was on my couch, and I obeyed you; and now you stumble over your own words according to which the remedy was ordered; and besides you have made me deaf.'"

8. Oyeb said: "When one has a spot or a cloudiness covering the eye or is blind, and 'Jericho was straightly shut up' [Joshua VI, 1, *i. e.*, the eye is tightly closed] and the doctor is consulted about the disease, he answers with pride and arrogance: 'Who is wise and able to explain this, and who, like me, in past or future, can interpret it? For those who suffer with their eyes, my knowledge reaches to the heavens, and for all humankind have I established my covenant. My wisdom is greater than that of the angels; when the sight becomes dim, I do wondrous work to clear it; I bring healing to the eye.' The patient's relatives honor him, they almost carry him on their hands. He visits with words of flattery and sits at the entrance of the house; he prepares in his hand the salt of Sodom and the poison of a serpent, thorns and thistles, makes a plaster of them and puts it on the eye; but this is as a sword and a spear, and the pain increases exceedingly and the patient cries bitterly, for his eye is blinded!"

CHAPTER III. FRIVOLITY

1. Oyeb said: "Concerning fevers in the humors, the physician will tell wonderful things to deceive people. He will proclaim all over the world, even to the islands: 'Whoever wishes to live, let him come unto me and I will give the right treatment; it has been prepared and and kept since the days before Ashmedai, the king of the demons. Hearken to me, O Nations, go and eat early in the morning and taste my bread [remedies]; it is valued as a food for great and mighty kings; the onion and the garlic mixed with straw, to be eaten in abundance with dry bread. Likewise, at midday and in the evening, you shall eat the meat of abominable, creeping animals, poultry or eggs. And likewise shall ye lie with women on a full stomach; this is a secret remedy and cure. This ye shall do and live from day to day and God will be with you, and He will not permit the destroyer to come into your houses. And whoever does not believe this, will do the opposite—"A man's folly will pervert his path." When it is rumored that the plague has begun to spread, we will send people to Gilead to seek for remedies, or for wine and beer in the cave of the two daughters of Lot, for their wine is from the vineyard of Sodom and from the fields of Gomorrah; a remedy is near at hand whose virtue and value no one can estimate. But if one's bad luck causes him to die, you need not weep, neither shall you pity him.'"

2. Oyeb said: "In liver or heart or lung diseases, the physician will say: 'I am an expert in their treatment, and I have acquired much wisdom and knowledge; this is known over all the world.' But in truth he is like an ass under a pack-saddle when he opens his mouth with words of frivolity. Instead of

wisdom they are [words of] stupidity and foolishness, and thus he says: 'For understanding of the liver, I surpass in knowledge and for heart disease there is no one like me except a dog; concerning diseases of the lung, who but I is sure that he knows of a wonderful cure? And on your giving me a trial, what will you find but that all the seven sciences are possessed by me?" And in truth, seven are the abominations in his heart and he has no conscience within him. Verily, while he continues in his self-flattery, the patient is in a critical condition; and though they find him to be ignorant, and put him to shame, yet will he not cease from his evil actions."

3. Oyeb said: "Go and see the doings of the physician and his remedies, for which he carries his sheaves [*i. e.*, fees]. He opens his mouth without limit, asserting that he knows all about diseases, accidents and their causes; he talks much about how to prepare aid and remedy. He goes to the druggist with pride, raises his hand to write, in order to show his ring. He prescribes in a foreign language, for his science is foreign to him; [he does this] in order to remove the crop with its feathers [in order to "bleed" the patient]; and between one word and the other he spits; this is his manner and habit. In unimportant matters he makes himself very busy. He says to the druggist: 'Take the liquid to the patient, charge him as much as you can, and ask for the pay, ere his lamp will be extinguished. And if he finds in it trouble and misery, we are innocent, since "all who spoil are exempted."'" Both rejoice in their prey, as people who have done charity. And what does it matter to them if the patient dies, for the earth will cover him! 'And what does it matter to us? We shall live on!'"

4. Oyeb said: "Listen, all ye people, to the words of the stupid quack who dwells in aristocratic places, when he says: 'I am descended from ancient kings, I am the son of sages, since the day that God created man. Who has secured even half of my knowledge in understanding the secrets of herbs, and of different drugs? Who knows their many high and low degrees? I know each one according to its name and place.'

"About bloodletting he will say: 'Did not my mind do all this? For I understand how to distinguish between good and bad hours and lucky and unlucky moments.' But he does not even know when it is new moon nor when it is full moon; he claims to know the days of bad omen, and that the day on which Haman was hanged is dangerous for bloodletting, unless it be for circumcision."

5. Oyeb said: "What a crime it is for the physician to speak foolishness in his ignorance and to extol himself with much wisdom. Woe unto such a shame! Woe unto such a disgrace! Even when one asks him about the limitations of medicine, he will answer arrogantly: 'Is any knowledge hidden from me? What sort of a question is this? There are two limits, you see, a limit on one side and a limit on the other side!' And if he is asked about fever, he will answer that this is a burning without fuel, coming hurriedly at different times one after the other. He will declare that the law [governing the fever] is hidden with the Lord; no man will ever know it. Concerning the beginning of the disease, its progress and disappearance, who can understand its nature and its duration and its end; all his words are void and vanity."

6. Oyeb said: "A physician's mistake leads to crime, quarrels and disputes. Of the dead he says that he is alive, and of the living that he is dead; there is no truth in his speech. He is the Reaper's agent; he is the assistant of the Angel of Death and his messenger; this is his function. He gathers medical books new and old and of many kinds to make a show of them, but not to read them. And if there are errors in them, he does not discover them; they remain where they are, there is no one to correct them. If he is asked about a chapter or a good treatise, he will put off the answer for the morrow, and at an opportune time he will say: 'Go away, go home, do you wish to examine me? Shall such a man as I answer fools? I am the physician who cures all maladies!'"

7. Oyeb said: "This is the way the present doctors slaughter, in order to get large fees and to be regarded as experienced. For the instructors announce: 'Whoever practices medicine without getting fees deserves to be stoned. Learn to make money by analogy from the Field of Ephron, [as Ephron, the son of Zohar, took from Abraham 400 silver shekalim to bury Sarah]; thus you will reap benefit and save. Go ahead and take for yourself, slaughter your sacrifice, and so eat [your fill]. Be ready to visit the patients, but not for mere talk or to be their aid and protector; for large compensation only and not for nothing! Here you have an example: King Hezekiah hid the book of medicine, because the physician did not get the reward of his labor. They would put off payment saying: 'Wait until Shiloh (Messiah) comes; go home in peace, but dare not to come here to ask for your reward.' Therefore, be careful in your practice, and do not come to the patient's house until you get your heave offering; and do not leave the house with empty hands, or with only some eggs or a piece of bread.'"

CHAPTER IV. DECEIT

1. Oyeb said: "Now let us describe all the remedies and their order, which were established in the days of Terah [father of Abraham] in Haran. A liquid medicine for fevers, and it is like sharp swords. Let there be taken roots of broom-bush and grass of nets, and the flowers of priesthood, from each one a part; a withered leaf and a leaf of thought, from each one an ounce or a pound; the shell of garlic, beans of the garden, a rod and a bullrush and foam also, from each one and a half pint, filled or empty; wasp's honey and the braying of an ass, and the threads of net; the mucus of the nose, the noise of millstones, from each one a handful; all this put in a pot, perforated or broken; let it be cooked with cursed water on the fire of hell [you can obtain it gratis] until it has boiled down one-half, and then it will be ready to drink. One bowl of foam and a pitcher of water let him drink at twilight.

[c] A Mishnaic law that exempts destruction of an object on the Sabbath from the penalty imposed for work done.

and let [the sick] taste of it at dawn. This cup of swords will empty him, without leaving a remnant until the intestines drop out; and, when he looks at the cup, his abdomen will swell.

2. "Another general remedy for all diseases: Let there be taken the mouth of a serpent, the noise of a storm, the blackness of the Ethiopian, the whiteness of women, oil of quarrel and contention, from each one-half measure; the tail of a lizard, the twittering of birds, the base of a camel's hump, the wings of flies, and the brain of a flea, and a whole fat tail, and the blossoms of shame and reproach; this you must cook; boil it in presumptuous water, with the eggs of lice, from each two kinds, in a boiling kettle full of crushed things and it shall be kept boiling until the water turns to vapor; let [the sick] drink it in the evening, morning and noon, and whether he will find a cure for his malady in the end will show, especially after his death."

3. Oyeb said: "This prescription will help in every fever, also in any illness or abscess: Take pure frankincense and powdered dust, thorns, soot of a furnace, and much smoke, from each one an equal measure with menstrual blood and the liquid part of fæces and thin dirt and fæces of wild foxes, from each one five shekels; oil of hypocrisy, and shame and reproach, and bitter spices, from each one a manah; perforated baskets, deadly venom of a poisoning snake, semen of evil doers, occipita of frogs, cow's dung and deadly flies, juice of brookstones, and soup of putrid flesh, of each one an equal weight; after the art of the apothecary shall they be mixed. All who eat it will do evil and will become heart-sick when they take it."

4. Oyeb said: "In the valley of weeping on the night of the Ninth of Ab, when the lamentations are being read, the doctors of the present day prepare the oil, to anoint the heads of the Am ha-Aretz [ignoramus] so they can fleece them: First take salt of Sodom, falsehood and deceit, poison of serpents and the head of an asp, and the water of those who have to bring offerings for transgression; nets and thorns of vineyards, and powdered dry grass, oil of burning, sweat of a tired person, from each one a tenth of an ephah. Together with all these, pound the wicked fool in a mortar, with crookedness; and this shall be the ointment. Whoever is rubbed with this will have sorrow and groaning instead of joy; he will have sickness instead of gladness, he will hope for cure, but, behold, there will be terror.

"This was written and signed by the scribe of the city; all of it by his strength and of his might; who can bear it, for it will be as a stumbling-stone? With it he will dig for himself his own deep grave."

CHAPTER V. PEACE

1. Oheb [the friend] said: "Now I repent, if I have spoken badly about the physicians, for I meant well! To wake their conscience; to make them study better their medical books [is my sole purpose]. Let them but be correct in their work and strong. Let them not waste their days in vanity and deceit. Let them walk before the people with courage; from this day on there shall be peace [between us]. I will tell no more of their shortcomings. From having been their foe, I will again become their friend; it is I who am speaking to them!"

2. Oheb said: "We are tired of many words. Let us make peace between us and become friends. If I have spoken till now because of my sorrow and anger, let friendship return and I myself shall lead it. If I have spoken too much, all will again be good and calm like the waters of Pishon. And you physicians, do your work diligently and with clean hands; and take for yourselves silver or gold, for the living must die and the dead will be restored to life. Seize fortune when it deals pleasantly with people. I have found a noted proverb, and it shall be as a sign to you: 'Good fortune comes not to the faithful man.'"

MINUTE ON THE DEATH OF DR. THEODORE C. JANEWAY

ADOPTED BY THE MEDICAL BOARD OF THE JOHNS HOPKINS HOSPITAL OF MONDAY, JANUARY 7, 1918, AND PRESENTED TO THE BOARD OF TRUSTEES

It is with a sense of sorrow and of personal loss that the Medical Board of The Johns Hopkins Hospital record the death of Theodore Caldwell Janeway, for a little more than three years the physician-in-chief to the hospital.

Dr. Janeway was a marked man from the beginning of his medical career. He was a lecturer in medicine first at the Bellevue Medical College and later at Columbia University where, in 1909, he was chosen Bard professor of medicine. He was at different times visiting physician to the City Hospital, St. Luke's Hospital and the Presbyterian Hospital in New York. In 1914, he was called to Baltimore to become professor of medicine in the university and chief of the medical clinic. In these positions he served until his death. Born on November 2, 1872, he died of pneumonia on December 27, 1917, at the early age of 45.

His natural medical ability he inherited as the son of a distinguished physician, but he acquired also from long and sympathetic association with his father a passion for medicine as an intellectual pursuit and an appreciation of it as a means of benefiting and assisting his fellow man. He was thus peculiarly fitted to serve as the head of a medical clinic, for to his great medical skill and judgment was added deep sympathy for suffering humanity.

The knowledge of medicine brought to him a sense of responsibility which was not to be satisfied solely by the treatment of patients under his care in the hospital or dispensary.

He keenly felt the economic and physical distress so frequently associated with and resulting from disease, and he gave to many charitable associations freely of his time and advice in the attempt to improve the condition of the unfortunate. He worked tirelessly and without regard for his health or strength.

A natural teacher, a clear, forceful expositor and an enthusiast that others should recognize the possibilities of medical science as well as the duties and obligations resting upon those skilled in medicine, he exerted a profound influence upon his students and associates and an influence that will not cease with his death.

Called into the service of the government in the spring of 1917, Dr. Janeway gave to the surgeon general's office his untiring efforts as befitted one with the high sense of patriotism that characterized him. The love of country led him to spend himself freely and to such an extent that he could not withstand the disease to which he fell a victim, young in years but having by precept and example influenced much the lives of many men.

PROCEEDINGS OF SOCIETIES

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY

OCTOBER 22, 1917

1. **Personal Observations of the Hopkins Unit in France.** JAY MCLEAN.

2. **Extracts from Letters from Various Members of the Hopkins Unit.**

NOVEMBER 5, 1917

1. **Adenoma of the Recto-Vaginal Septum.** DR. T. S. CULLEN. Published in the BULLETIN, November, 1917.

2. **Experiences in a Base Hospital.** DR. THOMAS MCCRAE.

It is always important to keep in mind that no one man sees all phases of disease in war; indeed, the great majority of men will see only one phase. Men in different places see different stages of the same disease. Practically all the patients in the base hospitals in England come from France, some only 36-48 hours from the trenches. My work was in an active general hospital of 2080 beds, with a number of associated convalescent hospitals, so that the service was constantly moving. One might think that to handle a service of 1000 medical or surgical patients would be difficult, but with proper methods it seemed little more difficult than the management of 100 beds.

In regard to the transport of the wounded, a message would come, for example, that 180 stretcher cases or 100 walking cases were on the way. The message would be received some hours ahead, and the convoy trains would come within five minutes of the specified time. The hospital trains are very well equipped, and the man in charge stops the train, when he wishes, for emergency cases. When the trains arrived, the stretchers were ready and the cases were assigned to the wards on the station platform. Every wounded patient carried on his coat a thick envelope of waterproof paper, on the outside of which was the diagnosis. There was enough on the card to indicate where the man belonged. The adjutant would look at the card and write on it the ward to which the man was assigned. The average time for a convoy of 120 stretcher cases was one hour from the time the train was in to the time the last man was in bed.

Among the diseases peculiar to war, we may first mention trench fever. This is absolutely new, so far as I could see. The vast majority of the cases come from the trenches, but a certain number have arisen back of the trenches. Statements are made that the disease has originated in hospitals in England among nurses and orderlies waiting on patients with the disease. I was told one case occurred in a nurse in the hospital where I was. I was able to prove that this was not so, and I could not find any one who had definitely seen such a case. The patients have an onset much like any other acute febrile disease. They feel badly for a day or two, have a good deal of headache, malaise, chills, fever and loss of appetite. The fever begins comparatively early and is not necessarily high. When those symptoms develop at the front, the men are sent down at once, and I saw some of them in about three or four days after the onset. In general, there is nothing particular in the examination, except one striking thing. They complain of pain, which is generally described as being in the shins. The fever is variable; it lasts sometimes five, six or seven days, sometimes only three or four, and then drops and the temperature runs along for some days at normal. After this interval of from 5-7 days, there is a sudden elevation in temperature, the fever going up to 102°-104°. This persists for 24 hours and then drops to normal. There is another afebrile period for 5-7 days, and then another paroxysm, the temperature again dropping to normal. That may go on for seven or eight attacks. The majority of the patients had two or three: after that the temperature was normal and there was no return of fever. With this elevation of temperature, there is apparently no increase in leucocytes. The pulse always goes up a little and the patient looks very ill. The point of particular interest is the condition in the legs called "painful shin." In the majority of cases the shin is very tender. In some cases when one goes near the bed, the man implores you not to touch it, a condition I have only seen otherwise in very severe cases of rheumatic fever. If you examine more carefully, you find that they often have tenderness behind the knees. Indeed, a good many of the patients had as much tenderness on pressure behind the knees as in the shins. After the period of fever is over, there is nothing left but this excruciating pain, which is usually worse at night; and it is very common to find these men sleeping during the day. Naturally, in such a condition, symptomatic therapy is of importance, but it was not very successful. Locally, the application of a solution of Epsom salts gave more relief than anything else. I was interested in trying the effect of sunlight. It acted like magic in some cases, but un-

fortunately they were the exceptions. Some of the patients were not affected at all. The views as to the etiology are conflicting and not one has been confirmed. A good deal of evidence points to the fact that the disease is carried by lice.

A second disease which one might say is peculiar to war, is the war nephritis, in which there certainly are seen features which are different from the ordinary acute nephritis seen in civil life. These cases usually have an acute onset. Many of them do not know anything is wrong until told by their comrades that their faces are swollen. Some begin with severe headache and others have to fall out on a march on account of dyspnœa; others feel weak and have pain throughout the body. In the early days edema is comparatively common, particularly of the face, and there is slight fever. One feels after watching these patients that such a case may go on indefinitely. It is called acute nephritis, but it goes on for week after week without any apparent change. The edema clears up fairly promptly. Uremia is not very common, although we had several patients brought in with it, who, when they left France, had apparently been well. After a few days, as the edema disappears, the patients feel better except for the persistence of excessive headache, which is generally relieved by lumbar puncture. The most persistent finding was blood in the urine, which went on indefinitely. It was not, as a rule, macroscopic after the first few days. There were a certain number of pus cells in nearly all these patients, and one curious thing was that the patients who had uremia were the ones who did the best. The duration in those cases was less than in the men who did not have uremia. The blood-pressure was not at all constant; in many there was a tendency to a rise during the day, often associated with the headache.

One naturally wonders what is at the bottom of these cases. A few are instances of an acute flare-up of an old nephritis, but these are only a small number. Again, one thinks of an infection from the throat. This has been studied pretty thoroughly, and it cannot be found except in a very small proportion. Pathologically, the features are exactly like those found after scarlet fever. In the majority of the cases the etiology is unknown.

One saw a certain number of cases of jaundice. We were hunting very busily for spirochætes, but did not find any. A number of cases resembled ordinary catarrhal jaundice; others were much more severe and one did not know what to call them.

One condition is going to worry every medical man in war service, and that is the cases of so-called soldier's heart. I saw nothing in these cases in any way peculiar to war. They were what we would ordinarily term cardiac neuroses, with perhaps a few additional points. There are nearly always some disturbed sensations referred to the heart. The patients often complain of pain which is a striking feature of the cases. In some there is breathlessness on any exertion and there is generally marked vasomotor disturbance, which is sometimes very striking. Examination shows very little. In a few there is evidence of dilatation, but in the great majority of cases you can find very little in the way of an actual objective sign.

There has been a great deal of discussion as to the cause of this condition. No doubt nervous strain plays a tremendous part. Physical strain did not seem to be a contributing factor. Perhaps a good deal of it might be attributed to tobacco. Smoking is almost constant, and nearly always cigarettes. The average runs from 20-40 a day. It is a serious question in the hospitals, where tobacco is issued as food is issued. It is a very difficult matter to cut down tobacco when it is being constantly served. If one goes into the history carefully, one is impressed by the number who have a susceptibility to tobacco. Some men regard smoking as the prime factor in these disturbances of the heart.

Of course, we looked for internal secretion disturbances, but they are nearly always conspicuous by their absence. A certain amount of infection may have played a part, but this is by no means invariable. In a few cases there had been damage to the heart beforehand, but there was no one thing that stood out. The more you observe them, the more you feel the tremendous importance of the nervous disturbance.

Of peculiar interest were the patients with gas poisoning. Early in the summer we got quite a number of gassed patients with what was designated as the "new gas." It was entirely different from any used before. A little later men spoke of it as "mustard gas." I asked many of them what they had noticed. Some had not noticed anything, but others said there was a smell of garlic. A few days later a chap came in who had been a chemist, and he said he was certain the smell was that of arsenic fumes. The men came in with varying symptoms. We had ten men come in together, who had been gassed at the same time with very different results. As a rule they felt nothing at the time. Sometimes there was constriction and difficulty in breathing, but the majority did not know they had been gassed. Some time afterwards, in from 2-3 hours to 2 days' time, the first symptoms appear, a profuse vomiting which lasts a few hours in some cases, in others for days. Many had irritation of the eyes, conjunctival redness and swelling, marked photophobia and inability to use the eyes in a light at all bright. That lasts a varying time, sometimes as long as 2-3 weeks. A few had corneal ulcer. In certain others, the brunt of the injury fell on the larynx. There were some very acute cases of laryngitis, with a good deal of cough, and in some patients marked bronchitis. Perhaps the most curious sign of all was the effect on the skin in certain of these patients. Some of them looked as if they had been stripped and some one had thrown mud on them in the center of the chest, and from there it had splashed all over them. There was nearly always pigmentation and of a remarkable appearance. Some desquamated very promptly, while others went on to an acute dermatitis. The Tommies called these lesions "gas burns." They began as a small bleb, which perhaps might increase until it was as large as the palm of one's hand. I saw no instance in which a soldier was apparently permanently damaged by this particular gas, although it is of course too early to say positively, except in some of the laryngeal cases. The eye conditions recovered perfectly. Some

of the men developed severe attacks of abdominal pain 2-3 weeks after being gassed, suggesting acute appendicitis. The first one I saw had rigidity, muscle spasm and great tenderness and it was a question whether he should be operated upon or not. However, the leucocytes were not increased and we waited; in 24 hours the pain had gone. There were a number of such cases.

The neurological side of the work is a subject upon which you might talk at great length. The two main problems are the injuries of the nervous system and the so-called war shock. Wounds of the head and nerves are simply bewildering. One of the great problems is as to when one should operate and when they should be left alone. Theoretically it may sound easy to decide, but it is a very difficult problem to settle. Among the patients with war shock some will talk frankly about what happened, some have no recollection at all, while others hesitate and you cannot get them to speak. It seems to me probable that in some of these shock cases there has been a certain amount of organic damage. One thing that harms the war-shock patients particularly is travel. A thunderstorm would excite them greatly. With lightning, they would often jump off the bed. If you could let one war-shock patient see another chap "acting up," he would usually subside and quiet down for an hour or two. We did not get a large number of these patients, but when a lot came in, we would generally try to pick out the most intelligent and work the matter out with him. In a certain number of cases, one got marked results. One patient lost all outward signs in about four days. This created a tremendous interest in the ward. We put him to work with other patients and he was the means of clearing up a number of the men who had come with him. When his condition had been explained to him, he said: "Why didn't I know that before? I see the whole thing now. If I had known before I went up to the front, I would never have been like this. I went up and heard a whole lot about shell shock and was all ready for it before it came." This particular man had been buried for a few minutes and came out with well-marked shock. With some cases it was impossible to do anything by analysis or suggestion. They have to have a certain amount of intelligence before one can do a great deal.

Mixed up with the whole subject of gas poisoning is aphonia. Many patients have difficulty with speech and a certain number are definitely hysterical, but I am not referring to them at present. Many patients who had been gassed, or who had had various disturbances, were left with aphonia. The majority improve slowly. Another thing which is extremely common is stammering. A great many of the men stammer, not necessarily the patients with war shock. It is striking to see how many in the wards are affected.

I mention one point because it is appearing quite often in the literature, and that is the cases with foreign bodies in the lungs. I am not speaking of the patients who need surgical treatment, but of those who have recovered and who have foreign bodies in the lungs. As you know, the French surgeons are strongly advocating operating on these patients. One hears that the mortality is rather high. The feeling in the Canadian service is strongly against operation. I saw a number and in the great majority you could find little in the way of signs. It seems bad practice to meddle with a condition which is not serious, at any rate at present, unless there are definite indications that one is going to make things better.

With regard to tuberculosis in the soldier, my feeling is that you cannot keep the standards up too high. To say as some men have said and written, that because a patient has had tuberculosis and has recovered is no reason why he should be rejected, seems to me to be absolutely wrong; and to say that men with pulmonary lesions that are not causing symptoms should be passed, appears to me to be abject nonsense. The man who has had tuberculosis should not be sent to the front line, although such men could be used back of the lines in many ways. Some writers claim that men with tuberculosis have done very well; perhaps they do, but when you think of them being constantly damp, sleeping in dugouts crowded as closely as possible, and often crowded into cellars, the conditions are certainly bad. In addition, the men with bacteria in the sputum are spreading infection; it could not be otherwise. My feeling is that the men who have had bronchitis or chronic emphysema should not go to the front lines. I do not believe that they should be passed as Class A men.

The medical officers who go to the front have some nice work ahead of them in diagnosing tuberculosis in the soldier. It is an entirely different matter from diagnosing tuberculosis in the civilian. The men have nearly all had bronchitis; they have nearly all lost weight. You hear that every one gains weight at the front; some do, but many have lost a great deal. With the bronchitis, they often have blood-streaked sputum, and there is also often slight fever. You get a man like that, particularly with signs of an old lesion at one apex, and what are you going to do about it? Many men with acute tuberculosis came back from the trenches with no fever, while the bronchitis patients did have fever. The X-ray plates did not help very much, because many patients showed marked shadows through the lungs. Then, again, you have not unlimited time to settle the matter; you have got to decide it promptly. As one senior medical officer said: "What we want in the men in charge is that they make decisions promptly. The man who handicaps us is the man who hesitates in making decisions." Now, how are you going to settle promptly cases like those I have mentioned? If the patient has tuberculosis, he ought to be sent home promptly; but we do not want to send back a chap who has a bronchitis that is going to clear up. The diagnosis of tuberculosis is one of the most difficult problems they have over there.

Another class of diseases is the gonorrheal infections and lues. The work in a war hospital gave me a big surprise in reference to them. There are more patients with lues in the medical service of hospitals in this country to-day, several times over, than in the general military hospital. Cases of active infection would not be seen in general hospitals. However, when one takes a 1000-bed service constantly full, one would expect a

considerable incidence. The only gonococcus cases were old infections and there were very few of those. Instances of lues were extremely rare. We always had a large number of Wassermann reactions done, and the amazing thing was to find how few were positive. Diagnoses made by the Wassermann were very occasional; indeed, there was nothing like the occurrence that one gets in an ordinary civil hospital. A certain number of the men had been most efficiently treated and showed negative reactions. The army treatment for lues is very thorough.

Just a note about the dental work. That was a very pleasant surprise. There are not many hospitals in this country to-day that are having anything like the grade of dental work done that was carried on in the military hospital to which I was attached. The whole staff was there all the time and any doubtful cases went to the chief at once. The mouth condition in the soldiers was much better than one would expect it to be. The men were taught to take care of their mouths, and it was a pleasure to see the way in which the dental work was done.

Mention should be made of the orthopedic work. American orthopedic men are largely responsible for the establishment of orthopedic centers attached to different hospitals. One cannot speak too highly of the work they are doing.

The X-ray work is a tremendous burden. The regulation is that any patient who may have a foreign body in him must be X-rayed, and with one or two hundred coming in at once, you may imagine the strain.

The mortality in the hospitals in England is surprisingly low. On the medical service where I was during the summer, there were four deaths, three from tuberculosis and one from pneumonia. There were no deaths from nephritis and none from gas poisoning. The deaths on the surgical side were also very few.

One point that comes up constantly is that of prognosis and this is most difficult to handle. Here is a man who comes in, and the question arises, "Is he likely to be well in a month, or will it take three or six months, and at the end of that time what sort of shape will he be in?" That problem comes up every day. With the Canadians, if the case was to be a long one, it was better to send him back to Canada. If he is going to get well, of how much use will he be? The problems are very much the same as those the American troops will have; and one must decide promptly as there are always patients waiting to come in. Another point is that it is so difficult to get experience. You discharge a man and send him on to a convalescent home and then you see no more of him. You cannot easily get data concerning him. Deciding wisely about the outlook for a patient is perhaps the most difficult problem of all.

The personal side is most interesting; it was a pleasure to spend as many hours as possible in the late afternoon and evening talking to the men. You could not get such a varied collection of men anywhere else. I often think of three adjacent beds in one of the wards. In one was a Montreal barrister, a graduate of an English university, in the next a typical Devonshire rustic, and in the third a Canadian Indian. It was impossible to get the men to talk much about what they had done, and not much about what they had seen. One of the most interesting groups came in one night, and just by chance about 20 beds in one ward were filled by men who had gone to France in August, 1914. When you saw those men you realized to some extent why that original force was able to do what it did. It was the first time that one or two of them had been back in three years. You could not get them to talk very much. They had, of course, been through all the terrible first days of the war. The thing that came out in talking with them was the fearful fatigue. As one chap put it: "You would get a chance to stop and you would drop there and feel that you could never get on your feet again. The whole thing now is just a blur of fatigue, beyond anything anybody could describe." Those were the chaps one felt like saluting for what they had done for every one of us.

They are great readers and devour books. What impressed me most was the amount of serious reading many of them were doing; collections of poems from many authors were extremely popular. It was surprising to find how much Shakespeare was read. Of course, they were not particularly keen on war literature.

The men are great collectors. One night when a convoy was coming in late, I saw the stretcher bearers having a hard time of it with one chap who had what appeared to be a considerable mass projecting on either side of the stretcher. The weight was so great they were obliged to put the stretcher down to rest. Across the foot was a great sack about 6 feet long, full at first sight of what appeared to be junk. The chap had collected helmets and all sorts of stuff. The wonder was how he ever got it through.

The personal side of the work was intensely interesting. The gratitude they had for what you were doing for them made you ashamed; it seemed so little compared with what they had done.

One important thing I would like to emphasize for the medical men who are going over. The first lesson a soldier learns is that of obedience and the second is how to wait. That lesson we all must learn. You cannot expect that the wounded and sick are going to come in at maximum all the time, although you have got to be prepared for the maximum. The medical organization has to be prepared for the largest possible volume of sick and wounded that can come at any given time. You can only do that by having many more men than are necessary for the average. Of course, the waiting is slow work, but it is one of the things that has to be learned.

The thing that made the strongest impression on me over there was the spirit of the men. I did not see the men at the front, but of the men in the hospitals nothing finer than the patience shown can be imagined. I cannot think of any one working in a war hospital for even a short time without coming away with his belief in the essential soundness of human nature strengthened.

NOVEMBER 19, 1917

1. **Studies on Blood Sugar.** Dr. Louis Hamman and Dr. I. Hirschman.

2. **Blood Cultures in Miliary Tuberculosis.** Dr. Mildred Clough. Published in the Bulletin, December, 1917.

3. **Auscultation of the Pulmonary Apices in Young Men.**[1] (Abstract.) Dr. John T. King, Jr., First Lieut., M. R. C.

The observations reported here were made during a recent examination for tuberculosis of about 22,000 troops at Chickamauga Park by a board of tuberculosis examiners. During the course of the work numerous men were found to present certain crackling sounds during auscultation, especially in the supraclavicular fossæ, which so closely simulated râles, that their identification became the most difficult problem that had to be solved. It was of importance to identify such sounds, because the board was authorized to disqualify any soldier who showed persistent moist râles in the upper lobes. During the latter part of the work the writer noted the frequency of adventitious sounds in the upper lobes in the examination of 819 men.

In 4 per cent of men examined crepitations were heard at or near one or more joints: the joints especially noted were the scapular, costo-sternal, and sterno-clavicular articulations and the shoulders anteriorly.

In 2.8 per cent certain crackles, usually rather loud and explosive, were heard for one or more respirations at the apices, disappearing promptly during continued breathing.

In 2.07 per cent were found the persistent apical clicks or crackles of the type that had proved so confusing.

No description of the last-named group of adventitious sounds was found in the usual text-books on thoracic diagnosis. Bushnell refers to a brief description of such crackles noted by Rosenbach over 40 years ago. He found them most often in muscular young men and children.

Joint crepitations may often be recognized by their groaning or grating quality. Confusing scapular sounds may be eliminated by one of three procedures: (1) By having the subject fold his arms and grasp the opposite shoulders with his hands; (2) by having him, while standing, bend the trunk forward to a horizontal position and allow the arms to hang limply downward; (3) by having him grasp an object at a level about as high as he can reach and exert enough weight on his arms to fix the scapulæ apart. Crepitations from the lateral sternal articulations may often be eliminated by having the subject throw his shoulders as far backward as possible.

Transient apical crackles, originating probably in the neck muscles, are often easily recognized by a loud, explosive quality. They are seldom reproduced by coughing.

The persistent apical crackles in healthy men are more difficult to distinguish from true râles than are any other adventitious sounds in the upper lobes. They are of every size, and occur singly or in sequence. Single clicks are usually of this type. All such crackles are most often heard when the subject holds his head in the position customary during examinations—slightly averted from the apex under examination. Such sounds often disappear if the chin is placed high in the air or if it is turned slightly toward the side that is being examined. These crackles are seldom increased by coughing, and usually occur during inspiration, but may be present in both phases of respiration. They are usually more intense when the stethoscope is directed medially, toward the neck muscles. Rosenbach reproduced such sounds by moving the neck muscles while the subject held his breath. Apical crackles of the above types almost certainly originate in the neck muscles and are of significance only in being differentiated from intrapulmonary râles.

[1] Published in *The Military Surgeon*, January, 1918.

NOVEMBER 23, 1917

On Two Fronts. Dr. Wilfred T. Grenfell.

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